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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,770		
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1 136(a) In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication
  If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U S C § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment See 37 CFR 1 704(b)

Status

1)☒ Responsive to communication(s) filed on *29 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) *3-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 January 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 2 January 2002 as the national stage of international application PCT/DE00/00693 filed 1 March 2000, which claims benefit of German patent application 199 09 357.1 filed 3 March 1999. The preliminary amendment filed 4 September 2001 has been entered. Claims 1-5 are pending.

Election/Restrictions

Applicant's election with traverse of Group II in the "Response..." filed 29 August 2003 is acknowledged. First, it should be pointed out that Applicant's assertion that claims 1-4, as amended in the 4 September 2001 paper, are directed to a method for prevention or treatment of Alzheimer's disease is in error. Amended claims 1 and 2 are directed to a method of treatment of Alzheimer's disease, while amended claims 3-5 are directed to a method of identifying a copper agonist which binds to the copper binding site of APP. Thus, only claims 1 and 2 are embraced by the elected invention (Group II) and claims 3-5 are embraced by non-elected Group III as set forth in the restriction requirement.

With regard to the restriction requirement set forth against Groups II and III, the traversal is on the ground(s) that Applicant's are no longer claiming a copper agonist which binds to the copper-binding site of the amyloid precursor protein and/or reduces or prevents release of Aβ peptide. Applicant asserts that as the claims are now directed to methods of preventing or treating Alzheimer's Disease using a copper agonist, and methods of identifying a copper agonist, Groups II and III share a technical feature that defines a contribution over the art. This is not found persuasive because, as pointed out by Applicant, "[t]he claims are directed to a method

of making and a method of using a copper agonist...The inventions are related by the special technical feature of the copper agonist" (29 August 2003 response, paragraph bridging pages 2-3). PCT Rule 13.2 requires that unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. In the instant case, the shared technical feature of the claimed methods is the copper agonist, regardless of whether or not the agonist is claimed. As the copper agonist does not represent a contribution over the prior art for reasons set forth in the previous Office Action, the claimed methods do not related to a single inventive concept.

Next, Applicant cites M.P.E.P. §803, and argues that the restriction requirement is improper because search and examination of the entire application can be made without serious burden. This argument is not found persuasive because: first, it is improperly based on rules governing U.S. restriction practice and not rules governing Unity of Invention according to those set forth in the Patent Cooperation Treaty; and second, restriction would still be proper under U.S. practice because Groups II and III embrace subject matter that could not be searched coextensively and therefore search and examination of the non-elected invention would impose a significant additional burden.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention. Claims 1 and 2 are under consideration herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

In the instant case, the claims are directed to a method of prevention or treatment of Alzheimer's disease comprising using a copper agonist which binds to the copper-binding site of the amyloid precursor protein and/or reduces or prevents the release of the amyloid Aβ peptide.

The Guidelines for Written Description state "The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (Federal Register, Vol. 66, No. 4, Column 1, page 1105). In the instant case, the copper agonist is clearly an essential element of the claimed method because it is the active ingredient in the composition

to be used. Thus, adequate written description of the claimed method requires that the full scope of the genus of compounds encompassed by the "copper agonist" of the claims be described.

The specification teaches that the copper agonist concerns any substance which can bind to the copper-binding site of APP and/or can reduce or prevent the release of the amyloid Aβ peptide (paragraph bridging page 3 and 4). The specification further teaches, "[c]opper agonists within the meaning of the present invention are also those substances which do not bind to the copper binding site but stabilize e.g. the conformation of APP which is characteristic of the copper APP complex, i.e. they can imitate the physiological effect of copper at other binding sites" (page 4). Thus, the copper agonist of the claims is generic to any molecule having the functional characteristic of binding to the copper binding site of APP or capable of reducing or preventing the release of the amyloid Aβ peptide.

The Guidelines for Written Description state: "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (*Id.*, at page 1106). "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406" MPEP §2163(3)(a)(ii).

In the instant case, the specification discloses two species having the characteristics of a copper agonist (i.e., Cu^{2+} and Zn^{2+}) and reduces these species to practice in an *in vitro* assay and a transgenic mouse model. However, the specification and claims make clear that the copper agonist encompasses compounds having highly divergent structural characteristics including oligopeptides, oligonucleotides, oligosaccharides, nucleotide analogs or low molecular natural substances isolated from microorganisms or plants. Thus, the two species of metal ions reduced to practice clearly fail to represent the full scope of genus of copper agonists. With regard to relevant, identifying characteristics, the specification teaches that the compounds "imitate copper mainly via their three dimensional structure and bind to the copper binding site" (page 4, lines 5-7) or "imitate the physiological effect of copper at other binding sites" (page 4, first full paragraph). However, the specification provides no description of the structural features that confer the recited function. The disclosure fails to describe the relevant identifying characteristics of a copper agonist because there is no teaching of the features that are unique to copper agonists other than a general recitation of function. Although the specification provides guidance as to how the skilled artisan might identify compounds having the function of a copper agonist (pages 5-9), an adequate written description of a copper agonist requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the copper agonist itself. It is not sufficient to define a copper agonist solely by its principal biological property (i.e., it binds to the copper binding site of the amyloid precursor protein and/ or reduces or prevents the release of amyloid Aβ peptide) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any copper agonist with that biological property. Also, naming a type of material

generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all copper agonists that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of any molecule having the functional characteristic of binding to the copper binding site of APP or capable of reducing or preventing the release of the amyloid Aβ peptide. Therefore, only the described copper agonists (i.e., Cu^{2+} and Zn^{2+}) meet the written description provision of 35 U.S.C. §112, first paragraph.

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to

make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claims are directed to a method of prevention or treatment of Alzheimer's disease comprising using a copper agonist, wherein said copper agonist binds to the copper binding site of the amyloid precursor protein and/or reduces the release of the amyloid Aβ peptide. As discussed herein above, the copper agonist of the claims encompasses a broadly divergent genus of compounds identified solely by a recitation of a desired function and some extremely broad general structural features such as divalent metal ion, oligopeptide, oligonucleotide, oligosaccharide, nucleotide analog, or low molecular substance from microorganisms or plants. Thus, the claims are directed to a method of using a vast number of unidentified compounds or the divalent metals Cu^{2+} or Zn^{2+} to prevent or treat Alzheimer's disease.

State of the prior art and level of predictability in the art: The relevant art provides examples of compounds having the properties of a copper agonist including Cu^{2+}, Zn^{2+} (see especially Borchardt (2000) *Cell. Mol. Biol.* 46:785-795) and certain urea derivatives (see Heinz *et al.* (U.S. Patent No. 5,814,646)). However, the art is silent with regard to other divalent metal ions, oligopeptides, oligonucleotides, oligosaccharides, nucleotide analogs, or low molecular substances from microorganisms or plants having the properties of a copper agonist. Furthermore, the art does not teach the skilled artisan the structural features of a copper agonist such that compounds having the functional properties of the copper agonist of the claims could be distinguished from compounds that do not have the functional properties of a copper agonist. Therefore, the skilled artisan must rely on the instant specification to teach how to obtain a

copper agonist such that the skilled artisan could practice full scope of the claimed method without undue experimentation.

With regard to treating or preventing Alzheimer's disease comprising administering a copper agonist, the art teaches that development of therapeutic agents that act by inhibition of amyloid Aβ peptide secretion is still in its early stages. Bachurin (2003) *Med. Res. Rev.* 23:48-88 teaches that, despite the theoretical promise of Aβ peptide inhibition as a therapeutic approach, as of 2003 there was no unequivocal evidence that Alzheimer's disease could be prevented or treated using an inhibitor of Aβ peptide formation (see the discussion entitled "*A. Inhibition of the Formation of APβ*" beginning on page 56). After an extensive review of available therapeutic approaches for Alzheimer's disease, Bachurin teaches, "a broad perspective for the design of medicines for the prevention and treatment of ND [neurodegenerative disease], primarily AD [Alzheimer's disease], does not correspond to the progress in this field" (page 78). Bachurin attributes this lack of progress to an insufficient understanding of the molecular and genetic mechanisms of the pathology and the absence of convenient and adequate models that have a high predictive ability for the selection of the most promising compounds. Thus, Bachurin casts doubt the ability of either the available theoretical knowledge or the available models to predict which compounds would be effective in the treatment of Alzheimer's disease.

Golde (2003) *J. Clin. Invest.* 111:11-18 concurs with the teachings of Bachurin, teaching that in spite of promising epidemiological data supporting a protective role for some agents, "[w]hether therapeutic intervention is likely to have a disease-modifying effect is much more controversial. Definitive insight into the temporal progression of AD is lacking" (page 15, paragraph bridging columns 1-2) and "[t]he major challenge that remains is to show that [anti-

Aβ] therapies actually alter cognitive decline in humans. The medical community should be cautious in evaluation the efficacy of anti-Aβ drugs, as they may not show such disease-modifying effects when given in therapeutic trials" (page 16, column 2). Likewise, Sano (2002) *Curr. Neurol. Rep.* 2:392-399 teaches, "[o]ne emerging theme is that results of clinical trials in AD do not match results of risk reduction reported in observational studies" (page 398, column 1). Thus, the art clearly teaches that epidemiological or preclinical evidence suggesting a compound might be effective in the treatment of Alzheimer's disease is far from predictive of clinical efficacy. Golde and Sano further teach that an important obstacle to obtaining effective therapy, particularly in using an anti-Aβ approach, is the absence of a clearly defined patient population that will respond to the treatment. Golde teaches that it is recognized in the art that Aβ accumulation precedes clinical cognitive impairment by many years and the trigger for the cognitive decline is unknown (page 15, paragraph bridging columns 1-2). Further, Golde teaches, "in AD, by the time a patient is symptomatic, Aβ-lowering therapies may not be effective" (page 16, column 1). Sano teaches that disappointing results obtained in AD patients "has led to the idea that once the disease is present, manipulation of the pathology cannot provide a benefit, and an inevitable cascade of deterioration is in place" (page 16, column 1). Thus, even if the skilled artisan is in possession of an effective Aβ-lowering compound, the art teaches that the patient population that would respond to such a compound is indefinite. Thus, the skilled artisan would not know to whom the compound should be administered without first engaging in experimentation to identify the population.

With regard to preventing or treating Alzheimer's disease using a copper agonist such as the species specifically disclosed in the specification, the art teaches that obtaining a prophylactic

or therapeutic effect by the method of administering Cu^{2+} or Zn^{2+} to an Alzheimer's disease patient is highly unpredictable. Although Constantinidis (1992) *Drug Dev. Res.* 27:1-14 report improvement in some Alzheimer's patients in a very limited trial of Zn^{2+} supplementation (see especially the discussion bridging pages 8-9). Several other articles, published well after the Constantinidis article, suggest that administration of Cu^{2+} or Zn^{2+} would actually have a deleterious effect. Borchardt *et al.* (2000) *Cell. Mol. Biol.* 46:785-795 (made of record in the IDS filed 4 September 2003) teaches, "bio-available Zn(II) seems to be an environmental risk factor for AD. A cognitive decline in AD patients was observed after Zn supplementation due to a disturbed iron-homeostasis" and "[i]n AD epsilon 4 apoE allele carriers significantly higher serum Zn concentrations were suggested to be an independent risk factor for development of AD" (page 793, column 2). Bush *et al.* (1994) *Science* 265:1464-1467 concurs with the teachings of Borchardt *et al.* stating, "'the clinical utility of Zn supplementation in the treatment of dementia has been advocated...despite the lack of evidence demonstrating benefit in AD subjects. In fact, a study of the effects of daily oral Zn supplementation in individuals with AD, as compared with supplementation in age-matched controls, demonstrated deleterious effects on cognition in the AD group in days" (page 1467, middle column, first full paragraph). Bush *et al.* suggests that Zn supplementation might adversely affect AD patients by promoting the aggregation of Aβ peptide (see throughout). In fact, Finefrock *et al.* (2003) *J Am. Geriatr. Soc.* 51:1143-1148 teaches that the current (i.e., as of 2003) hypothesis is that age related abnormalities of copper and iron, as well as zinc homeostasis induce the aggregation and toxicity of β-amyloid (see the sections entitled "COPPER", "IRON" and "ZINC" beginning in the second column of page 1143). Finefrock then goes on to indicate that metal chelating agents, which have

the effect of decreasing the levels of free Cu^{2+} and Zn^{2+} in an patient, have shown promise as therapeutics for treatment of Alzheimer's disease in their own right (see especially the section entitled "Chelating Agents" on page 1146).

When viewed as a whole, the art provides very little guidance to enable the skilled artisan to obtain the vast majority of compounds alleged to be useful in the claimed method, and indicates that developing a method for the prevention or treatment of Alzheimer's disease is far from routine, even when the putative therapeutic has demonstrated activity that might prove beneficial. This is at least in part because the art is yet to identify a patient population that is responsive to therapeutic agents such as the instant copper agonist. Furthermore, with regard to copper agonists such as Cu^{2+} or Zn^{2+} the art suggests that the claimed method would actually adversely affect many Alzheimer's disease patients. Given that the art indicates that effective treatment of Alzheimer's disease would be highly unpredictable, the skilled artisan must rely on the specification to set forth the method of treatment in adequate detail, such that the claimed method could be practiced without the requirement for undue experimentation.

Amount of direction provided by the inventor and existence of working examples: The instant specification teaches that divalent metal ions such as Cu^{2+} and Zn^{2+} are copper agonists and teaches *in vitro* assays that can be used to identify other compounds having the function of a copper agonist (*Id.*). The specification does not provide a single example of an oligopeptide, oligonucleotide, oligosaccharide, nucleotide analog, or low molecular substances from a microorganism or plant having the properties of a copper agonist and does not set forth any teachings that would allow the skilled artisan to distinguish compounds that meet the limitations of a copper agonist from those compounds that do not meet the limitation without blind trial and

error experimentation to make and test each compound having the structure of an oligopeptide, oligonucleotide, oligosaccharide, nucleotide analog, or low molecular substances from a microorganism or plant.

With regard to methods of preventing or treating Alzheimer's disease, the specification merely provides that administration of Cu^{2+} or Zn^{2+} to a cultured Chinese hamster ovary cell line and a transgenic mouse expressing the human Aβ peptide reduced Aβ production (see especially Examples 3 and 6). The specification provides no evidence that administration of Zn^{2+} or Cu^{2+} or any other copper agonist has any effect at all on the clinical manifestations of Alzheimer's disease and provides no teachings that would address the myriad of obstacles facing the skilled artisan seeking to practice a method of preventing or treating Alzheimer's disease comprising using a copper agonist. Thus, the teachings of the specification fail to cure the deficiencies of the art.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to make the full scope of the claimed invention without undue experimentation. In *In re Wands*, the court states, "[t]he determination of what constitutes undue experimentation in a given case requires the application of standard reasonableness, having due regard for the nature of the invention and the state of the art" (at 1404). In the instant case, practicing the claimed invention commensurate with its full scope requires possession of the copper agonist to be used in the method. The art provides only very limited examples of compounds having the properties of a copper agonist which are the same as those disclosed in the instant specification. The specification then sets forth broad general classes of compounds from which copper agonists

might be isolated, which compounds encompass an almost infinite number of structurally unrelated molecules, and instructs the skilled artisan to test each compound to see if it can be used in the method. Clearly, given the nature of the invention and state of the art, the amount of experimentation required to practice the full scope of the instant claimed invention is undue according to standard reasonableness.

Furthermore, extending the teachings of the specification such that the claimed method could be practiced with any copper agonist would clearly require a level of experimentation beyond what is considered routine in the art. The art clearly teaches that, in spite of promising leads, very few compounds have shown to be effective in the treatment of Alzheimer's disease and copper agonists such as Cu^{2+} and Zn^{2+} are likely to adversely affect many Alzheimer's disease patients. Furthermore, the art does not provide a single established example of effective prevention of Alzheimer's disease. The teachings of the specification provide only that administration of Cu^{2+} and Zn^{2+} to cultured cells and a transgenic animal reduces production of Aβ, which, in theory, might be beneficial to a patient with Alzheimer's disease. Given no more than this, and in view of the undeveloped nature of the art relevant to using copper agonists as therapeutics in Alzheimer's disease, the skilled artisan would not be able to practice the claimed method without resorting to blind trial and error experimentation to identify an patient population that could be treated according to the claimed method and establish how a copper agonist might be used such that a prophylactic or therapeutic effect could be achieved.

Thus, due to the art recognized unpredictability of preventing or treating Alzheimer's disease using a copper agonist and the lack of guidance in the specification or prior art with

regard to how to practice the claimed method, it would require undue experimentation to practice the invention over any scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in the recitation of "using a copper agonist" in the second line of claim 1. Given its broadest reasonable definition, the term "using" means only the act or practice of employing something. As "using" is not defined in the specification in any more specific terms, the claims are directed to a method of treatment comprising employing a copper agonist in some undefined way. Thus, the method steps encompassed by the claim are unclear.

Claim 2 is additionally indefinite in the recitation of "low molecular natural substance". A low molecular substance is not a term of art and the specification provides no definition of what constitutes a low molecular natural substance (see page 4, lines 13-14). Therefore, the limitation is indefinite.

Claim 2 is additionally indefinite in limiting the copper agonist to a "chemical substance library". The specification (page 3, third full paragraph) defines a copper agonist as a substance. According to the most applicable definition it appearing in the Merriam-Webster dictionary (online edition) a substance is "matter of particular or definite chemical constitution". As a chemical substance library would by definition comprise many different substances and have

indefinite chemical constitution, the identification of a library of substances as a copper agonist would seem incongruous with the definition provided in the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Note: The following rejections apply to the extent that the prior art discloses the same method embraced by the instant invention. The prior art rejection is not to be construed as an indication that the claimed or anticipated methods are *enabled* for the wide breadth of subject matter potentially embraced by the claimed method. As the requirements for enablement under 35 U.S.C. §112, first paragraph, and anticipation under 35 U.S.C. §102 are distinct (see *In re Hafner* 161 USPQ 783 (CCPA 1969)), finding that claims both lack an enabling disclosure and are anticipated by the prior art is not a contradictory position.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Heinz *et al.* (U.S. Patent No. 5,814,646).

Heinz *et al.* teaches a method of protecting a warm blooded mammal for the progression of Alzheimer's disease comprising administering an effective amount of a urea derivative that is capable of inhibiting the production of Aβ in whole cells. As the urea derivative meets the limitation of a copper agonist, to the extent that it encompasses an agent that reduces or prevents

the release of amyloid Aβ peptide, the method of Heinz *et al.* is the same as the instant method. The claim is therefore anticipated by the teachings of Heinz *et al.*

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Constantinidis (1992) *Drug Dev. Res.* 27:1-14.

Constantinidis teaches a method of treating Alzheimer's disease comprising administering a zinc-containing compound, which is disclosed in the instant application as a copper agonist (see especially the discussion bridging pages 8-9). Thus, the method of Constantinidis comprises all of the limitations of the instant claimed method. Further, the copper agonist of Constantinidis meets the limitations of the divalent metal ion of claim 2. Therefore, the method of Constantinidis anticipates the method of claims 1 and 2.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DMS

DAVID M...
PRIMARY EXAMINER